.45g/100 ml = 78 mEq/L Na^+

Role of osmolality and plasma volume during rehydration in humans

HIROSHI NOSE, GARY W. MACK, XIANGRONG SHI, AND ETHAN R. NADEL
John B. Pierce Foundation Laboratory and Departments of Epidemiology and Public Health and Physiology, Yale University School of Medicine, New Haven, Connecticut 06519

NOSE, HIROSHI, GARY W. MACK, XIANGRONG SHI, AND ETHAN R. NADEL. *Role of osmolality and plasma volume during rehydration in humans.* J. Appl. Physiol. 65(1): 325–331, 1988.—To determine how the sodium content of ingested fluids affects drinking and the restoration of the body fluid compartments after dehydration, we studied six subjects during 4 h of recovery from 90–110 min of a heat [36°C, <30% relative humidity (rh)] and exercise (40% maximal aerobic power) exposure, which caused body weight to decrease by 2.3%. During the 1st h, subjects rested seated without any fluids in a thermoneutral environment (28°C, <30% rh) to allow the body fluid compartments to stabilize. Over the next 3 h, subjects rehydrated ad libitum using tap water and capsules containing either placebo (H_2O-R) or 0.45 g NaCl (Na-R) per 100 ml water. During the 3-h rehydration period, subjects restored 68% of the lost water during H_2O-R, whereas they restored 82% during Na-R ($P < 0.05$). Urine volume was greater in H_2O-R than in Na-R; thus only 51% of the lost water was retained during H_2O-R, whereas 71% was retained during Na-R ($P < 0.05$). Plasma osmolality was elevated throughout the rehydration period in Na-R, whereas it returned to the control level by 30 min in H_2O-R ($P < 0.05$). Changes in free water clearance followed changes in plasma osmolality. The restoration of plasma volume during Na-R was 174% of that lost. During H_2O-R it was 78%, which seemed to be sufficient to diminish volume-dependent dipsogenic stimulation. These results suggest that the poorer rehydration when drinking water is caused by both removal of the osmotic drive for drinking and a rise in free water clearance, primarily due to the loss of electrolytes during dehydration. In addition, the higher degree of recovery in plasma volume than in total body water during H_2O-R and Na-R delayed rehydration by removing the volume-dependent dipsogenic stimulation.

involuntary dehydration; osmotic balance; electrolyte loss; fluid compartments

HUMANS have a prolonged period of delayed rehydration after thermal dehydration. This phenomenon has been known as involuntary dehydration since 1947 (25), and a number of studies have been conducted to better understand its cause (8, 10, 13). Dill et al. (3) suggested that thirst is primarily a function of the sodium chloride concentration in plasma rather than plasma volume. Greenleaf (9) stated that two factors unique to humans contribute to the involuntary dehydration: excessive extracellular fluid loss due to Na^+ loss into sweat and the upright posture. Recently, Morimoto et al. (16) found that the degree of involuntary dehydration in humans was reduced when a glucose-electrolyte solution rather than water was ingested during and after thermal dehydration. However, their results may have been biased by the presence of glucose in their rehydration solution because taste of the glucose-electrolyte solution may have influenced drinking behavior. More recently, Nose et al. (21, 22) demonstrated that the degree of involuntary dehydration was reduced in rats supplied with water containing 0.45 or 0.9% NaCl to compensate for the loss of electrolytes during thermal dehydration. These results strongly suggest the involvement of osmotic factors in the involuntary dehydration phenomenon.

There has been other evidence demonstrating the importance of the plasma volume change in involuntary dehydration. Nose et al. (21) reported that in rats 17–20% of the ingested water remained in the vascular space, which is twice as much as expected, assuming that ingested fluid is distributed proportionally among the body compartments. These results also suggested to us that the high retention of ingested fluid in the vascular space might diminish volume-dependent dipsogenic stimulation despite the incomplete restoration of the total water deficit.

The purpose of this study was to assess the involuntary dehydration phenomenon in humans. We wished to examine the distribution and fate of the water ingested during rehydration to determine the mechanisms contributing to the high retention of ingested fluids in the vascular space. Our hypothesis was that the disproportionately high recovery of plasma volume, with respect to total body water, contributes to the removal of the dipsogenic drive. Furthermore, removal of the osmotic stimulus accompanying plasma volume dilution limits the rate of body fluid restitution.

METHODS

Design. Six male volunteers were studied. Their physical characteristics are shown in Table 1. With a few exceptions, to be described below, the procedures and analytic techniques were the same as in the preceding communication (18). We induced a dehydration of 2.3% body wt by exposing subjects for 90–110 min to a simultaneous heat [36°C, <30% relative humidity (rh)] and exercise (40% maximal aerobic power) stress in the seated position.

After dehydration, a 60-min recovery without fluid was imposed to allow the body fluid compartments to stabi-

TABLE 1. *Characteristics of subjects*

	Age, yr	Wt, kg	$\dot{V}O_{2\,max}$, ml·kg^{-1}·min^{-1}	Blood Volume, ml/kg	Plasma Volume, ml/kg
Mean	28.3	68.3	51.8	82.1	47.4
Range	23–33	56.5–83.7	36.4–62.9	61.0–102.3	33.5–61.4

n = 6 subjs. $\dot{V}O_{2\,max}$, maximum aerobic power.

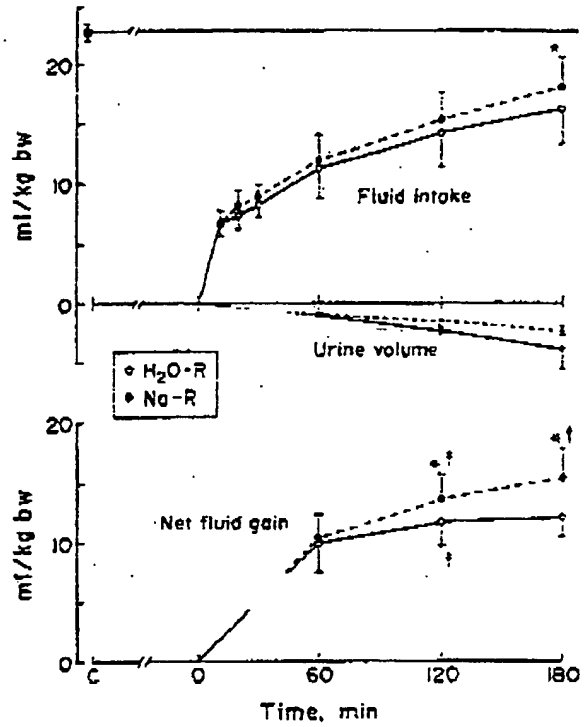

FIG. 1. Cumulative amount of fluid intake, urine volume, and net fluid gain during 180 min of rehydration. Values are means ± SE of 6 subjects. ■, Body water loss as difference from prerehydration level. ○ and ●, Tap water (H_2O-R) and NaCl (Na-R) recovery conditions, respectively. * H_2O-R vs. Na-R ($P < 0.05$); ‡ 60 vs. 120 and 180 min ($P < 0.05$).

lize. Recovery was in a thermoneutral environment (28°C, <30% rh) and subjects were in the seated position throughout. A butterfly catheter was inserted into a superficial forearm vein within 10 min of the termination of exercise. Blood samples were taken directly after catheter placement and at 30 and 60 min of recovery. There were no differences in plasma osmolality (P_{osmol}) or plasma volume between 30 and 60 min after the termination of exercise, thereby confirming that a new steady state had been achieved.

During the next 180 min, subjects rehydrated with water plus capsules ad libitum. Two series of rehydration experiments were performed on each subject: *1*) with tap water (H_2O-R), and *2*) with 0.45% NaCl solution (Na-R). Subjects were given a capsule containing either 0.2 g sucrose/100 ml water during H_2O-R or 0.45 g NaCl/100 ml water during Na-R. Water temperature was ≅ 15°C. The minimum allowable drinking volume at a time was 100 ml because subjects were expected to take one capsule per 100 ml. Sodium and potassium concentrations in tap water were undetectable by flame photometry and the osmotic activity of the sucrose solution was ~4% of the 0.45% NaCl solution, so that the gain of osmotically active substances in H_2O-R was ignored. Ingestion of salt in capsule form was necessary to avoid any influence of taste on drinking behavior.

Blood samples were taken at 10, 20, 30, 60, 120, and 180 min of the rehydration period, and urine was collected at 60, 120, and 180 min of rehydration.

Measurements. From each blood sample we determined P_{osmol} (freezing point depression, model 3DII, Advanced Instruments) and plasma electrolytes ($[Na^+]$ and $[K^+]$, flame photometry, Instrumentation Laboratory model 433; $[Cl^-]$ Cotlove chloride titrator). These were expressed in meq/kg H_2O after correction for plasma solids. We also measured microhematocrit, hemoglobin concentration (cyanomethemoglobin), plasma protein concentration (refractometry), and plasma solid concentration (dry weight method).

Calculations. Total water loss due to dehydration was estimated from body weight loss. Net fluid gain was calculated by subtracting total urine loss from water intake, assuming that respiratory water loss and sweat loss at rest were negligible. Electrolyte losses in sweat and urine due to dehydration were calculated by multiplying the volume of water loss by the concentration of each fluid, respectively (see Ref. 18). Net electrolyte gain was calculated by subtracting electrolyte loss in urine from electrolyte intake. The change in plasma volume (ΔPV) during an experiment was calculated from changes in hematocrit and hemoglobin concentrations (4). The change in extracellular fluid (ΔECF) space after 180 min of rehydration was determined by Cl^- distribution, assuming that Cl^- is equally distributed throughout the ECF space (22)

$$\Delta Cl^-_{ECF} = Cl^-_{In} - Cl^-_{U} - Cl^-_{S}$$

$$\Delta Cl^-_{ECF} = \Delta Cl^-_{ISF} + \Delta Cl^-_{Pl}$$

$$\Delta ISF = 1/1.05 \times \Delta Cl^-_{ISF}/\Delta Cl^-_{Pl} \times \Delta PV$$

$$\Delta ECF = \Delta PV + \Delta ISF$$

$$\Delta ICF = \Delta TW - \Delta ECF$$

where ICF denotes intracellular fluid space, ISF denotes interstitial fluid space, TW indicates total body water, and subscripts Pl, ISF, ECF, In, U, and S indicate plasma, interstitial and extracellular fluid spaces, intake, urine, and sweat, respectively.

Statistics. Two-way analysis of variance (ANOVA) for repeated measures was used to determine differences between H_2O-R and Na-R, with significant differences between the two groups at various times determined with Tukey's minimum significant difference (MSD) test (27). Specific trend analysis for each treatment was performed with a one-way ANOVA for repeated measures with significant differences between each time also determined with Tukey's MSD test. The null hypothesis was rejected when $P < 0.05$. Regression formulas were calculated by Brace's method (1). All values are reported as means ± SE of six subjects.

RESULTS

The total body water deficits immediately before rehydration in the two conditions (H_2O-R and Na-R) were

23.7 ± 0.9 and 21.7 ± 1.0 ml/kg body wt. Since the difference in deficit between the two conditions was not significant, the data were pooled and the body water loss during dehydration therefore averaged 22.7 ± 0.7 ml/kg body wt ($n = 12$).

Figure 1 shows the cumulative amounts of fluid intake, urine output, and net fluid gain during rehydration. The cumulative fluid intake increased sharply for the first 30 min in both recovery conditions and then slowly increased to 16.1 ± 2.9 ml/kg body wt in H_2O-R and 17.8 ± 2.8 ml/kg body wt in Na-R after 180 min of rehydration. By 180 min the cumulative fluid intake for Na-R was significantly greater than for H_2O-R. Urine volume tended to be greater during H_2O-R than Na-R, but this difference was not statistically significant. Taking the urine volumes into account, the net fluid gain at 180 min was 15.3 ± 2.4 ml/kg body wt in Na-R and 12.1 ± 1.6 ml/kg body wt in H_2O-R. The difference in net fluid gain was significant at 120 and 180 min. Net fluid gain during Na-R increased significantly between 60 and 180 min, whereas net fluid gain during H_2O-R showed no significant increase after 60 min.

Figure 2 shows the changes in hematocrit (ΔHct), hemoglobin concentration (ΔHb), and plasma solids during rehydration. After 60 min of rest without fluids after dehydration, Hct, Hb, and plasma solids were increased significantly. These variables returned to control relatively slowly during H_2O-R; Hct was restored after 30 min of rehydration and Hb and plasma solids were restored after 120 min of rehydration. On the other hand, these variables returned to the control levels more rapidly during Na-R than during H_2O-R, with significant differences being maintained between the two rehydration conditions throughout the 180 min. During Na-R, Hct fell significantly below the control values after 120 min. Changes in plasma protein concentration were almost identical to changes in plasma solids. Total protein content, calculated from plasma protein concentration and PV, was 3.4 ± 0.2 g/kg before dehydration in both groups and, at 180 min of rehydration, 3.4 ± 0.3 g/kg and 3.5 ± 0.2 g/kg in H_2O-R and Na-R, respectively.

Figure 3 shows the changes in plasma electrolytes during rehydration. During Na-R, plasma electrolytes tended to decrease, but P_{osmol} remained significantly above the control concentration until 120 min of rehydration, [Na^+] until 60 min, [K^+] until 30 min, and [Cl^-] until 10 min. On the other hand, plasma electrolytes

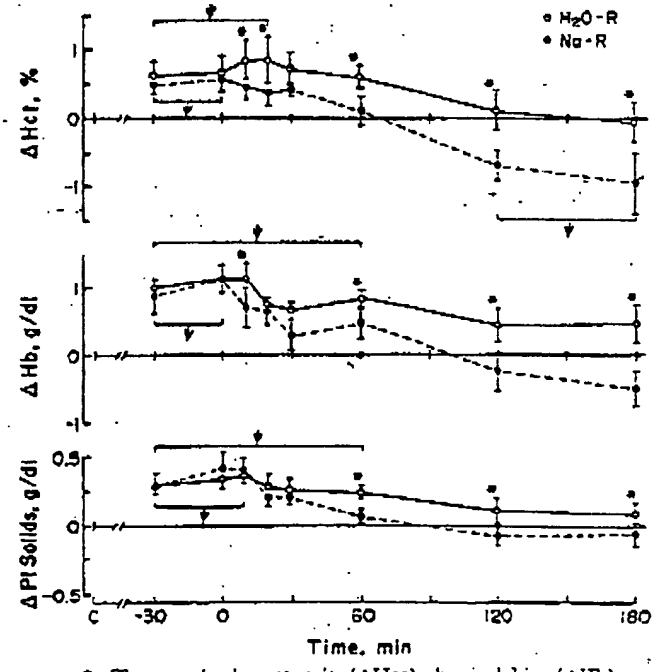

FIG. 2. Changes in hematocrit (ΔHct), hemoglobin (ΔHb), and plasma (ΔPl) solids shown as differences from control values (C). Symbols and other abbreviations as in Fig. 1. ψ Different from control. ($P < 0.05$).

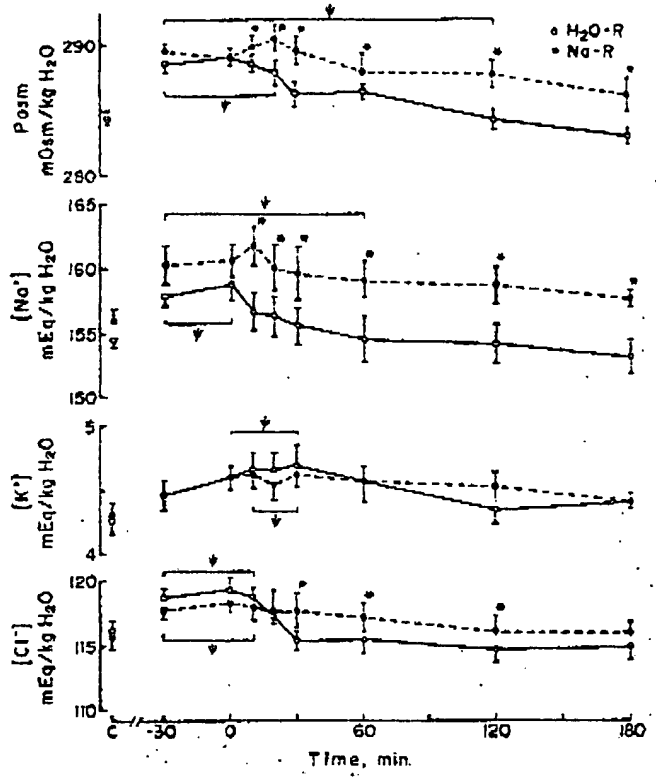

FIG. 3. Osmolality (P_{osm}) and Na^+, K^+, and Cl^- concentrations in plasma during rehydration. Symbols and other abbreviations as in Figs. 1 and 2.

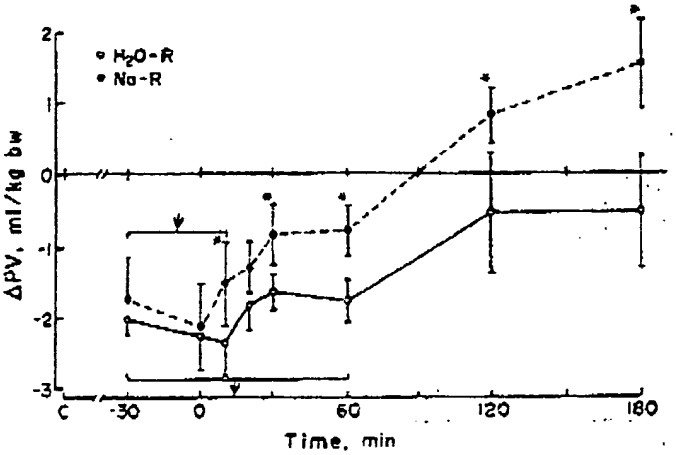

FIG. 4. Changes in plasma volume (ΔPV) shown as differences from control values. Symbols and other abbreviations as in Figs. 1 and 2.

decreased significantly at the beginning of H_2O-R, and significant differences between the two conditions were maintained for P_{osmol} and $[Na^+]$ throughout the rehydration period. No significant differences in $[K^+]$ occurred between the two conditions throughout the rehydration period.

Figure 4 shows the changes in plasma volume from predehydration values. After dehydration, the PV deficit was 2.28 ± 0.51 and 2.14 ± 0.60 ml/kg body wt in the H_2O-R and Na-R experimental conditions, respectively. During H_2O-R, PV increased slowly but remained significantly lower than the control PV until 60 min. PV restoration was faster during Na-R and returned to the control level by 20 min. By 180 min of rehydration, the changes in PV with respect to control were −0.51 ± 0.8 and +1.58 ± 0.63 ml/kg body wt in H_2O-R and Na-R, respectively.

Free water clearance (C_{H_2O}) was significantly increased (less negative) during H_2O-R but decreased slightly (more negative) in Na-R (Table 2). These differences in C_{H_2O} between the recovery conditions were significant. In addition, the loss of osmotically active substances and osmotic clearance (C_{osmol}) was greater in Na-R than in H_2O-R (Table 2).

During Na-R subjects consumed 119% of the Na^+ lost during dehydration, whereas during H_2O-R they consumed no electrolytes. Because of the K^+ and Na^+ losses in urine during rehydration, the net cation balance at the end of the rehydration period was −0.66 meq/kg body wt in Na-R, whereas it was −1.81 meq/kg body wt in H_2O-R (Table 3).

Fluid and electrolyte balances during rehydration are summarized in Fig. 5. The means are plotted with SE bars at 60-min intervals from the dehydrated condition (0 min) to rehydrated conditions (60, 120, and 180 min) in both groups. The intersection of the x- and y-axes represents the predehydrated condition (control) and the solid line indicates the isotonic line, $y = 0.15x$. The area above the isotonic line reflects hypertonic body fluids and the area below the line represents hypotonic body fluids. In both recovery conditions, H_2O-R and Na-R, fluid and electrolyte balance moved toward the theoretical isotonic line. Only in H_2O-R did the fluid balance reach the isotonic line. The degree of involuntary dehydration after 180 min of drinking was primarily determined by the cation deficit.

Changes in the body fluid compartments after dehydration and 180 min of rehydration are summarized in Fig. 6. The values are shown as differences from the predehydration values. After dehydration and after the 60-min period of body fluid stabilization, change in total body water (ΔTW), change in intracellular fluid space (ΔICF), ΔECF, and ΔPV were −22.7 ± 0.7, −10.2 ± 1.0, −12.6 ± 0.8, and −2.2 ± 0.4 ml/kg body wt, respectively. After 180 min of rehydration the fluid deficits in all compartments were significantly reduced. The TW and ICF space were still significantly lower than predehydration values in both recovery conditions. The ECF space recovered in Na-R, whereas it did not in H_2O-R. Significant differences between H_2O-R and Na-R occurred in ΔTW, ΔECF, and ΔPV (Fig. 6).

Figure 7 shows the relationship between the recoveries in PV (rPV) and total body water (rTW) (*top*) and between the rPV and ECF space (rECF) after 180 min of rehydration (*bottom*). Values are shown as differences from the prerehydration values in each subject, and the means of each group with SE bars are also shown.

Since there were no significant differences between the regression formulas between the recovery conditions, all data were pooled for the following analysis. The rPV was closely correlated not only with the rTW ($y = 0.47 \times x - 3.8$; $r = 0.77$, $P < 0.01$), but also with the rECF space ($y = 0.48 \times x - 1.09$; $r = 0.87$, $P < 0.001$) during rehydration. The ratios of rPV to rECF were not significantly different between the two groups during rehydration, averaging 0.36 ± 0.11 and 0.29 ± 0.04 for H_2O-R and Na-R, respectively, but the ratio of rPV to rTW was significantly greater in Na-R (0.21 ± 0.05) than that in H_2O-R (0.12 ± 0.05).

The dashed lines in Fig. 7 (*top* and *bottom*) are the theoretical lines, assuming that the distribution of ingested fluid between the two compartments was proportional to their initial volumes (28). All the data points except three are located above the theoretical lines, which

TABLE 2. *Renal function after dehydration and rehydration*

	Dehydration	Rehydration, min		
		60	120	180
Urine flow, $\mu l \cdot kg^{-1} \cdot min^{-1}$				
H_2O-R	9.7±1.6	8.9±0.9	21.0±11.4	25.9±17.2
Na-R	9.0±1.2	8.4±1.3	11.5±2.8	12.1±3.5
$[Osmol]_U \times$ urine flow, $\mu osmol \cdot kg^{-1} \cdot min^{-1}$				
H_2O-R	7.9±0.9	8.6±0.9	8.2±1.0	7.1±0.7
Na-R	7.5±0.5	7.5±0.5	9.3±1.3	9.3±1.0*
C_{osmol}, $\mu l \cdot kg^{-1} \cdot min^{-1}$				
H_2O-R	27.5±3.0	29.9±3.2	28.7±3.5	25.3±2.6
Na-R	25.9±1.7	26.1±1.8	32.4±4.4	33.9±3.0*
C_{H_2O}, $\mu l \cdot kg^{-1} \cdot min^{-1}$				
H_2O-R	−17.8±2.2	−21.0±2.4	−7.7±11.1	0.6±16.2
Na-R	−16.9±1.2	−17.7±1.3	−21.0±4.2*	−21.7±3.8*

Values are means ± SE. H_2O-R and Na-R, rehydration conditions with tap water and 0.45% NaCl solution, respectively; $[osmol]_U$, urine osmolality; C_{osmol}, osmotic clearance; C_{H_2O}, free water clearance. * Significant differences between H_2O-R and Na-R groups ($P < 0.05$).

TABLE 3. *Electrolyte balance after dehydration and at 180 min of rehydration*

	Dehydration		Rehydration	
	H_2O-R	Na-R	H_2O-R	Na-R
Na^+ loss	−1.01±0.15	−1.18±0.12	−1.28±0.17	−1.48±0.13*
K^+ loss	−0.31±0.03	−0.31±0.03	−0.54±0.05	0.58±0.03*
Cl^- loss	−0.95±0.11	−1.09±0.14	−1.28±0.12	−1.53±0.16*
Na^+ intake				+1.40±0.22
Cation balance	−1.32±0.15	−1.49±0.13	−1.51±0.17	−0.66±0.14*

Values are means ± SE in meq/kg body wt. H_2O-R and Na-R, rehydration conditions with tap water and 0.45% NaCl solution, respectively. * Significant differences between H_2O-R and Na-R ($P < 0.05$).

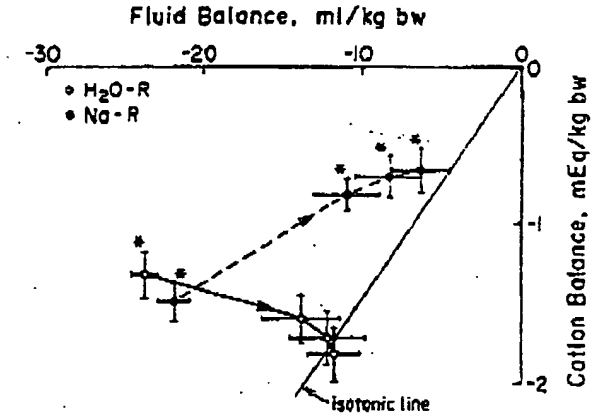

FIG. 5. Recoveries of fluid and electrolyte balance during rehydration. Means of 6 subjects are shown with SE bars of 60-min intervals during rehydration. ——, Theoretical isotonic line ($y = 0.15x$). * Points significantly different from isotonic line ($P < 0.05$). Abbreviations as in Fig. 1.

means a greater relative recovery of PV than TW or ECF space.

DISCUSSION

It is well known that the regulation of fluid intake is influenced by both P_{osmol} and volume, as well as by oropharyngeal and gastric factors (5, 24), but the relative importance of these factors in rehydration remains unknown. Since the early phase of rehydration is the time during which water and electrolytes move dynamically among fluid compartments to attain new steady states, transient changes in P_{osmol} and/or PV might influence drinking behavior.

Drinking: the early phase of rehydration (0–60 min). Even though the changes in P_{osmol} and PV were quite different between H_2O-R and Na-R until 60 min of rehydration (Figs. 3 and 4), fluid intake and net fluid gain were identical during this period (Fig. 1). During H_2O-R, P_{osmol} and $[Na^+]$ began to decrease immediately after the onset of drinking. $[Na^+]$ returned to the control level within 10 min and P_{osmol} returned by 30 min. During Na-R, P_{osmol} remained elevated after 60 min. Thus if an elevated P_{osmol} were the only factor contributing to the dipsogenic drive, drinking should have been greater during Na-R. PV restoration at 60 min of H_2O-R was only 17% of that lost, whereas at 60 min of Na-R, PV restoration was 60% of that lost. Thus the rates of fluid intake

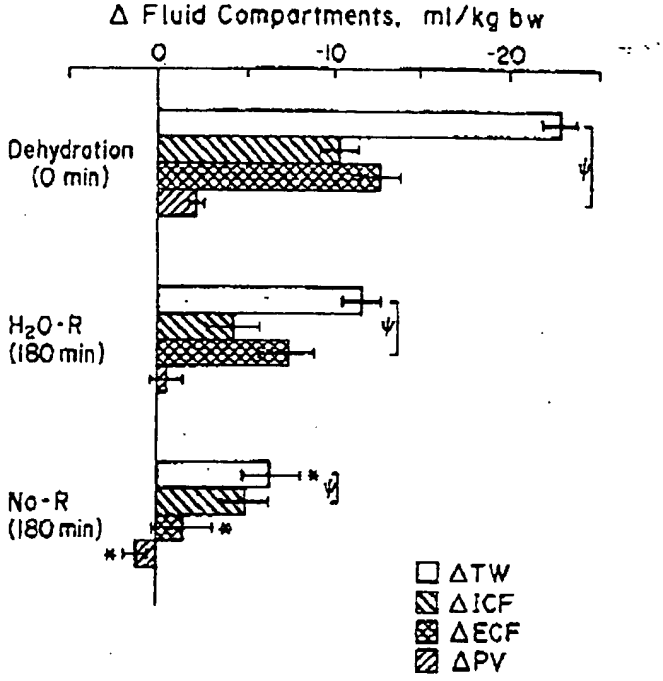

FIG. 6. Changes of fluid compartments shown as differences from control values. Values are means ± SE of 12 subjects in dehydration and 6 subjects in each recovery condition at 180 min of rehydration. All recovery values are significantly different from dehydration values ($P < 0.05$). * Tap water (H_2O-R) vs. NaCl (Na-R) recovery conditions ($P < 0.05$); † different from control ($P < 0.05$). ΔTW, change in total body water; ΔICF, change in intracellular fluid space; ΔECF, change in extracellular fluid space; ΔPV, change in plasma volume.

in the different recovery conditions, while similar, were driven by different factors.

Other occurrences may have further contributed to the similarity in the rates of fluid intake despite the apparent differences in volume and osmotic drives in the two recovery conditions. The importance of preabsorptive influences, such as oropharyngeal metering and gut distension in the early termination of drinking, have been reported by several investigators (e.g., 24). Thrasher et al. (29) reported that in dogs oropharyngeal stimuli were important not only for the inhibition of drinking but also for the suppression of arginine vasopressin release. Similar results have been reported in humans (7, 26). Rolls et al. (23) suggested the importance of gut distension in the early termination of fluid intake based on subjective feelings reported by the subjects.

Drinking: the later phase of rehydration (61–180 min). Significant differences in fluid intake between H_2O-R and Na-R occurred at 180 min and in net fluid gain at 120 and 180 min. P_{osmol} and $[Na^+]$ in Na-R remained elevated at 120 min. On the other hand, in H_2O-R P_{osmol} returned to the control level by 30 min. The increase in urine flow and C_{H_2O} in H_2O-R after 120 min reflected the return of P_{osmol} to its control level, thereby causing net fluid gain to remain constant. During Na-R subjects restored PV to the control value by 30 min; during H_2O-R PV was restored by 120 min.

Thus two issues should be considered in attempting to understand the greater cumulative fluid intake at 180 min during Na-R. The first is the persistent existence of an osmotic drive for drinking in Na-R and the early

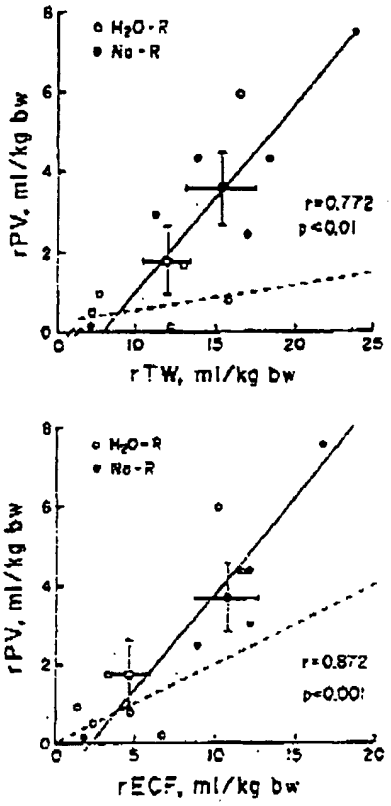

FIG. 7. Relationship between recoveries in plasma volume (rPV) and total body water (rTW) (*top*) and between recoveries in plasma volume (rPV) and extracellular fluid volume (rECF) (*bottom*) during rehydration with tap water (H_2O-R) and 0.45% NaCl solution (Na-R). ——, Theoretically expected lines, assuming that distribution of ingested fluid between two compartments is proportional to their initial volumes (Ref. 28). Individual data at 180 min of rehydration are plotted as differences from prerehydration values, as are means ± SE of each group.

removal of this drive in H_2O-R. The second is that the PV recovery in the H_2O-R seemed to be sufficient to diminish the volume-dependent dipsogenic drive. In support of this latter notion, we found that plasma renin activity and plasma aldosterone returned to control levels by 180 min in H_2O-R (19).

The fluid and electrolyte status in H_2O-R returned to the theoretical isotonic line by 60 min of rehydration (Fig. 5). At this time the subjects still had a 49% deficit in TW, of which 64% was attributed to inadequate replacement of ECF and 36% to inadequate replacement of ICF (Fig. 6). During Na-R subjects almost returned to the isotonic line by 180 min, and they did so closer to the origin. After 180 min the deficit to TW was 30%, which was nearly all attributed to the ICF deficit, since the subjects regained 95% of the Na^+ loss (Table 3). After 180 min the ICF space deficits were 4.2 and 5.3 ml/kg body wt ($P > 0.05$) in H_2O-R and Na-R (Fig. 6), and the K^+ losses were 0.54 and 0.58 meq/kg body wt, respectively (Table 3). In other words, the ICF space losses had an average $[K^+]$ of 130 meq/kg H_2O in H_2O-R and 110 meq/kg H_2O in Na-R. Thus 70–80% of the lost ICF space can be explained by the movement of water after the loss of K^+, assuming that $[K^+]$ in ICF is initially 165 meq/kg H_2O (22). These results indicate that the ICF space deficit in both recovery conditions was almost entirely due to the K^+ loss. The larger ECF space deficit in H_2O-R was due to the greater loss of Na^+. In other words, the degree of rehydration in each compartment was determined by the ability to restore the ions lost from each compartment.

Recovery of PV. Costill and Sparks (2) reported that rehydration with a glucose-electrolyte solution resulted in a better recovery of PV than with tap water after thermal dehydration. Mack et al. (13) obtained similar results using dilute NaCl solutions. In this study, we found increases in PV of 1.6 and 3.5 ml/kg body wt after 180 min in H_2O-R and Na-R, respectively. This was equivalent to 12 and 21% of the net fluid gain and 36 and 29% of the increases in ECF space, respectively (Fig. 7). It is reasonable to assume that the greater restoration of PV in Na-R was simply due to the greater restoration of the ECF space. Another possibility is that the gut absorption rate of a hypotonic NaCl solution may have been faster than that of tap water. Nose et al. (21) reported that rats rehydrated with 0.45% NaCl solution tended to regain blood volume more rapidly than with tap water. Maximum changes in blood volume occurred 14 min after the onset of rehydration when drinking tap water and 9 min after the onset when drinking the NaCl solution. Hunt and Pothak (11) investigated the effects of solutes on gastric emptying in resting humans and demonstrated that gastric emptying was three times faster when subjects drank a dilute saline solution (100–300 mosmol/kg H_2O) than when drinking distilled water. An improved gastric emptying may contribute to a more rapid restoration of blood volume when subjects drink dilute saline.

Figure 7 shows that the recovery of PV after 180 min of rehydration was relatively greater than the recovery of TW in both recovery conditions. The recovery of PV was also greater than the recovery of the ECF (Fig. 7, *bottom*). Although the precise reason for the selective retention of ingested fluid in the vascular space is not clear, the movement of fluid between the intra- and extravascular compartments should follow the Starling forces (6, 12, 15). The time to reach a steady state depends on the transvascular filtration coefficient for water, which is influenced by the available capillary surface area in different conditions (14, 17). Nose et al. (20) reported that after thermal dehydration in rats, the splanchnic blood volume was well maintained, in contrast to that of skin and muscle. It is possible that a redistribution of blood flow to maintain the central blood volume changes the effective capillary surface area and influences fluid movement between intra- and extravascular spaces during rehydration. Thus the rate of blood volume restoration should be determined by both the rate of fluid movement from the gastrointestinal tract to the intravascular space and the rate of fluid shifts between the intra- and extravascular spaces. The selective retention of ingested fluid in the vascular space may have diminished the volume-dependent dipsogenic stimulation in spite of the persistent existence of a TW deficit.

In summary, during recovery from moderate (2.3% body wt) whole-body dehydration, a delay in rehydration is caused by both the electrolyte deficit from the intra-

and extracellular spaces and the removal of a volume-dependent dipsogenic drive due to the selective retention of ingested fluid in vascular space.

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REFERENCES

1. BRACE, R. A. Fitting straight lines to experimental data. *Am. J. Physiol.* 233 (*Regulatory Integrative Comp. Physiol.* 2): R94–R99, 1977.
2. COSTILL, D. L., AND K. E. SPARKS. Rapid fluid replacement following thermal dehydration. *J. Appl. Physiol.* 34: 299–303, 1973.
3. DILL, D. B., A. V. BOCK, AND H. T. EDWARD. Mechanism for dissipating heat in man and dog. *Am. J. Physiol.* 104: 36–43, 1933.
4. ELKINTON, J. E., T. S. DANOWSKI, AND A. W. WINKLER. Hemodynamic changes in salt depletion and in dehydration. *J. Clin. Invest.* 25: 120–129, 1946.
5. FITZSIMONS, J. T. *The Physiology of Thirst and Sodium Appetite.* Cambridge, UK: Cambridge Univ. Press, 1979.
6. GAUER, O. H., J. P. HENRY, AND C. BERN. The regulation of extracellular fluid volume. *Annu. Rev. Physiol.* 32: 547–595, 1970.
7. GEELEN, G., L. C. KEIL, S. E. KRAVIK, C. E. WADE, T. N. THRASHER, P. R. BARNES, G. PYKA, C. NESVIC, AND J. E. GREENLEAF. Inhibition of plasma vasopressin after drinking in dehydrated humans. *Am. J. Physiol.* 247 (*Regulatory Integrative Comp. Physiol.* 16): R968–R971, 1984.
8. GREENLEAF, J. E., AND F. SARGENT II. Voluntary dehydration in man. *J. Appl. Physiol.* 20: 719–724, 1965.
9. GREENLEAF, J. E. Dehydration-induced drinking in humans. *Federation Proc.* 41: 2509–2514, 1982.
10. GREENLEAF, J. E., R. J. BROCK, L. C. KEIL, AND J. T. MORSE. Drinking and water balance during exercise and heat acclimation. *J. Appl. Physiol.* 54: 414–419, 1983.
11. HUNT, J. N., AND J. D. POTHAK. The osmotic effects of some simple molecules and ions on gastric emptying. *J. Physiol. Lond.* 154: 254–269, 1960.
12. ISOGAI, Y., H. NOSE, K. MIKI, AND T. MORIMOTO. Dynamics of fluid movement between intravascular and interstitial spaces. *J. Theor. Biol.* 100: 305–317, 1982.
13. MACK, G. W., X. SHI, AND E. R. NADEL. Human rehydration following exercise in the heat (Abstract). *Med. Sci. Sports Exercise* 18, *Suppl.*: S73, 1986.
14. MIKI, K., T. MORIMOTO, M. NOSE, H. ITOH, AND S. YAMADA. Canine blood volume and cardiovascular function during hyperthermia. *J. Appl. Physiol.* 55: 300–306, 1983.
15. MORIMOTO, T., K. MIKI, H. NOSE, H. TANAKA, AND S. YAMADA. Transvascular fluid shift after blood volume modification in relation to compliances of the total vascular bed and interstitial fluid space. *Jpn. J. Physiol.* 31: 869–878, 1981.
16. MORIMOTO, T., K. MIKI, H. NOSE, S. YAMADA, K. HIRAKAWA, AND C. MATSUBARA. Changes in body fluid and its composition during heavy sweating and effect of fluid and electrolyte replacement. *Jpn. J. Biometeorol.* 18: 31–39, 1981.
17. NOSE, H. Transvascular fluid shift and redistribution of blood in hypothermia. *Jpn. J. Physiol.* 32: 831–842, 1982.
18. NOSE, H., G. W. MACK, X. SHI, AND E. R. NADEL. Shift in body fluid compartments after dehydration in humans. *J. Appl. Physiol.* 65: 318–324, 1988.
19. NOSE, H., G. W. MACK, X. SHI, AND E. R. NADEL. Involvement of sodium retention hormones during rehydration in humans. *J. Appl. Physiol.* 65: 332–336, 1988.
20. NOSE, H., T. MORIMOTO, AND K. OGURA. Distribution of water losses among fluid compartments of tissues under thermal dehydration in the rat. *Jpn. J. Physiol.* 33: 1019–1029, 1983.
21. NOSE, H., M. MORITA, T. YAWATA, AND T. MORIMOTO. Recovery of blood volume and osmolality after thermal dehydration in rats. *Am. J. Physiol.* 251 (*Regulatory Integrative Comp. Physiol.* 20): R492–R498, 1986.
22. NOSE, H., T. YAWATA, AND T. MORIMOTO. Osmotic factors in restitution from thermal dehydration in rats. *Am. J. Physiol.* 249 (*Regulatory Integrative Comp. Physiol.* 18): R166–R171, 1985.
23. ROLLS, B. J., R. J. WOOD, E. T. ROLLS, H. LIND, W. LIND, AND J. G. G. LEDINGHAM. Thirst following water deprivation in humans. *Am. J. Physiol.* 239 (*Regulatory Integrative Comp. Physiol.* 8): R476–R482, 1980.
24. ROLLS, B. J., AND E. T. ROLLS. *Thirst.* Cambridge, UK: Cambridge Univ. Press, 1982, p. 88–110.
25. ROTHSTEIN, A., E. F. ADOLPH, AND J. H. WILLIS. Voluntary dehydration. In: *Physiology of Man in the Desert*, edited by E. F. Adolph et al. New York: Interscience, 1947, p. 254–270.
26. SECKL, J. R., T. D. M. WILLIAMS, AND S. L. LIGHTMAN. Oral hypertonic saline causes transient fall of vasopressin in humans. *Am. J. Physiol.* 251 (*Regulatory Integrative Comp. Physiol.* 20): R214–R217, 1986.
27. SOKAL, P. R., AND F. J. ROHLF. *Biometry.* New York: Freeman, 1981, p. 349–354, 246–247.
28. SPECTOR, S. W. *Handbook of Biological Data.* Philadelphia, PA: Saunders, 1956, p. 340.
29. THRASHER, T. N., J. F. NISTAL-HERRARA, L. C. KEIL, AND D. J. RAMSAY. Satiety and inhibition of vasopressin secretion after drinking in dehydrated dogs. *Am. J. Physiol.* 240 (*Endocrinol. Metab.* 3): E394–E401, 1981.